

REMARKS

Claims 2-17, 25, 29, 38, 44-61 and 65-107 are now pending.

Claims 4-17, 25, 29, 38, 44-61, 66-73, 79-89, 98-105 and 107 have been withdrawn.

Minor typographical errors have been corrected in Claim 3, line 25; Claim 106, line 30, where a period is replaced with a comma.

In the previous amendment, allowed Claim 65 has been put in an independent form reciting all the limitations of its parent claim. In the course of that amendment an unnecessary limitation, to wit: the non-SOD mimic, was erroneously added to the claim. That limitation is deleted by the instant amendment.

Claims 2 and 106 are the only other independent claims.

Claims 2 and 106 have been amended to recite a Markush group consisting of non-metallic polyamines and only two metallic ones, namely, chromium and vanadium polyamines, in order to distinguish the claimed invention from Abrams et al. newly cited by the examiner.

The chromium and vanadium polyamines of Examples 17 and 18 are the only metallic compositions disclosed or prescribed in the disclosure.

The reference discloses only the ruthenium complex of cyclam as a regulator of nitrous oxide in very remote connection with the treatment of diabetes.

Abrams et al. describes the synthesis of Ruthenium metal complexes. By contrast the present patent application discloses and claims the composition, synthesis and utility of polyamines and substituted polyamines, which except for chromium and vanadium complexes are non-metallic compounds. The substitution reactions to add the side groups in the compounds are different from the synthesis of metal chelates. Abrams et al. states that ruthenium and osmium complexes attenuate NO production and indicates that this may be

used to treat vascular / pressor diseases such as septic shock, post-ischaemic cerebral damage, migraine and dialysis induced renal hypertension, immunopathologic diseases such as hepatic damage in inflammation and sepsis, allograft rejection, graft versus host diseases, diabetes and wound healing; neurodegenerative diseases such as cerebral ischaemia, trauma, chronic epilepsy, Alzheimer's disease, Huntington's disease, and AIDS dementia complex; and side effects of treatment such as restenosis following angioplastic treatment and secondary hypertension following cytokine treatment, without any prior art or experimental demonstration of effective treatment of diabetes by this type of compounds. Further the presumed efficacy of such a mechanism of action to treat any or all of these diverse diseases may be considered in light of the absence of development of any such compound clinically for such therapeutic purpose.

Thus, Abrams et al. teaches that ruthenium and osmium complexes treat diverse diseases but do not indicate that a polyamine or a metal such as chromium or vanadium treat these diseases by attenuation of nitrous oxide production. Nowhere does the reference describe a mitochondrial class of diseases or any supposed relationship between mitochondrial diseases and nitrous oxide levels.

The disclosure extensively teaches the role of polyamines in treating mitochondrial diseases resulting from acquired mitochondrial DNA damage and inherited mitochondrial DNA damage as recited in claims 2 and 65. Although not specifically recited in the claims, it teaches the inhibition of mitochondrial enzymes as well as the function of vanadium as an analog of phosphate groups with capacity to inhibit tyrosine phosphatases and chromium as an agent, which exerts therapeutic benefit in diabetes and cardiac dysmetabolic syndrome by altering body mass ratio. The disclosure also describes extensively the toxicity of free metals such as iron, zinc,

cadmium, cobalt, mercury as catalysts in damaging mitochondrial DNA and also the possibly damaging effects of excess zinc and inert metals such as xenon and tin in degenerative diseases and further describes how the chemistry of polyamines may be optimized to remove excess free metals on a general or selective basis during the treatment of individual mitochondrial diseases.

Accordingly, the three independent claims, not only recite invention clearly distinct from either Abrams et al. or Riley et al., thus overcoming the rejection under 35 USC 102(b), but also define fundamental and non-obvious differences with the cited prior art beyond the norms of 35 USC 103 . Indeed the invention teaches away from Abrams et al., taking a completely opposite approach to the use of metal complexes.

Claim 75 has been amended to correct an indefiniteness regarding “said compounds”.

Claim 77 and 78 have been amended to avoid any inference that the selected polyamine composition is one which falls outside the limitation of amended Claim 2, and to clearly recite that the heat of formation is used to assure that the selected polyamine composition will not deplete metal by binding to those metal ions.

Claim 106 has been amended to add the formulae erroneously left out in the last amendment.

Claim 106 has further been amended to recite only three types of polyamines, namely, diamines, triamines and tetramines, in order to distinguish the claimed invention from Riley et al. which discloses larger molecules, namely, pentamines.

Support for the three classes of small-molecule polyamines can be found at 20:34-64 of the incorporated patent No. 5,906,996; and in the substitutions specified in connection with the formula given in the Abstract.

The Examiner is urged to call the undersigned if necessary, in an attempt to resolve any other outstanding issue.

Respectfully submitted.



John D. Buchaca
Registration No. 37,289
1545 Hotel Circle South, Suite 150
San Diego, CA 92108-3426
Telephone: 619 294 2922
Fax: 619 294 8674

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on December 16, 2004, by John D. Buchaca, Reg. No. 37,289.

Signature: _____



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